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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,299	10/09/2001	Yoshiya Gunji	212289US0PCT	4922

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AJINOMOTO CORPORATE SERVICES, LLC
INTELLECTUAL PROPERTY DEPARTMENT
1120 CONNECTICUT AVE., N.W.
WASHINGTON, DC 20036

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,299	GUNJI ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,7-10 and 12-31* is/are pending in the application.

4a) Of the above claim(s) *14,15,18,19 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7-10,12,13,16,17,20,21 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/4/2005 has been entered.

[2] Claims 1-2, 5, 7-10, and 12-31 are pending in the application.

[3] Applicants' amendment to the claims, filed 1/4/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicants' arguments filed 1/4/2004 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity/Rejoinder

[6] In view of applicants' amendment to the claims, it is noted that claims 16-17 and 20-21 now share a same or corresponding special technical feature with the elected

claims. As such, claims 16-17 and 20-21 have been rejoined with the claims of the elected invention.

[7] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are being examined on the merits.

[8] Claims 14-15, 18-19, and 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claim to Priority

[9] Applicants' claim for foreign priority under 35 USC § 119(a)-(d) to Japanese applications 11/103143, filed 4/9/1999, 11/169447, filed 6/16/1999, and 11/368097, filed 12/24/1999, is acknowledged. Certified copies of the foreign priority documents have been filed in the instant application on 10/9/2001.

Information Disclosure Statement

[10] All references cited by applicants in the information disclosure statements (IDSs) filed January 10, 2002, October 21, 2002, May 15, 2003, and September 05, 2003 have been considered by the examiner. A copy of each IDS was attached to the Office action mailed 2/23/2004.

[11] If the examiner has inadvertently overlooked an IDS that has previously been filed in the instant application, applicants' cooperation is requested in alerting the examiner to this IDS in the response to this Office action.

Specification/Informalities

[12] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --*Methylophilus methylotrophus* Having Enhanced Dihydrodipicolinate Synthase and/or Aspartokinase Activity for L-Amino Acid Production--.

Claim Objections

[13] Claims 2, 5, 7, 9, 12, 16, 20, 26, and 28 are objected to for the following reasons:

[a] Claim 2 has an underline symbol between "strain" and "according."

[b] Claims 5 and 7 are grammatically incorrect in the recitation of "nucleotide sequence comprising a nucleotide numbers" in lines 13-14 of claim 15 and lines 5-6 of claim 7. It is suggested that applicants replace the term with, for example, "nucleotide sequence comprising nucleotide numbers."

[c] Claim 9, although clear in its meaning, is awkward in the recitation of "...introduction into cells of said DNA sequence..." It is suggested that applicants replace the term with, for example, "...introducing into cells said DNA sequence..."

[d] Claims 12 and 28 are grammatically incorrect in the recitation of "producing an L-lysine." It is suggested that the term be replaced with, for example, "producing L-lysine."

[e] Claims 16 and 20 are grammatically incorrect in the recitation of "a protein which has an amino acid sequences..." It is suggested that the term be replaced with, for example, "a protein which has an amino acid sequence..."

[f] The term "dihydrokipicolinate reductase" in claim 26 is misspelled and should be replaced with, for example, "dihydrodipicolinate synthase."

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[14] Claims 16-17 and 20-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a DNA. The claims read on a product of nature and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[15] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 1 (claims 12-13 and 26 dependent therefrom), 5 (claims 8-9 and 28-29 dependent therefrom), and 7 (claims 2, 10, 27, and 30-31 dependent therefrom) are rejected as being unclear in the recitation of "hybridizes." The specification indicates

that the "stringent" condition as recited in claims 1, 5, and 7 is "a condition that allows hybridization under a washing condition of usual Southern hybridization" (p. 36, lines 9-10). "Current Protocols in Molecular Biology" (Ausubel et al., John Wiley and Sons, Inc., New York, 1993, Unit 2.9A) discloses that Southern blotting is "the transfer of DNA fragments from an electrophoresis gel to a membrane support." However, the "hybridization" as recited in the claim would appear to be a hybridization reaction *following* a Southern transfer. Clarification is requested. If applicants intend for the hybridization to follow Southern transfer, it is noted that it is unclear as to the scope of nucleic acids that are encompassed by parts b) of the claims as there is no indication as to the length of time for the step of "washing." It is customary in the art to provide a specified length of time for a hybridization reaction. See "Current Protocols in Molecular Biology" (Unit 2.10), regarding *Length of prehybridization and hybridization incubations,* which teaches, "[t]he protocols recommend prehybridization for 3 hr with nitrocellulose and 15 min for nylon membranes. Inadequate prehybridization can lead to high backgrounds, so these times should not be reduced. They can, however, be extended without problem. Hybridizations are usually carried out overnight. This is a rather sloppy aspect of the procedure, because time can have an important influence on the result, especially if, as described above, an excess amount of a single-stranded probe is being used. The difficulties in assigning values to the parameters needed to calculate optimum hybridization time has led to the standard "overnight" incubation, which in fact is suitable for most purposes. The exception is when hybridization is being taken to its limits, for instance in detection of single-copy sequences in human DNA, when longer

hybridization times (up to 24 hr) may improve sensitivity if a single-stranded probe is being used. Note that this does not apply to double-stranded probes, as gradual reannealing results in only minimal amounts of a double-stranded probe being free to hybridize after ~8 hr of incubation" (underline added for emphasis). Thus, one of skill in the art would recognize the dependence of time as being a critical parameter in determining the scope of nucleic acids that bind under certain hybridization conditions. It is suggested that applicants clarify the meaning of the claims.

[b] Claim 9, which depends from claim 5, recites "...dihydrodipicolinate synthase that does not suffer from feedback inhibition by L-lysine..." and "...aspartokinase that does not suffer from feedback inhibition by L-lysine." However, it is noted that there is no antecedent basis in claims 5 or 9 for such dihydrodipicolinate synthase or aspartokinase that does not suffer from feedback inhibition by L-lysine as recited in claim 9. It is suggested that, for example, applicants delete the term "does not suffer from feedback inhibition by L-lysine" in claim 9.

[c] Claims 12 (claim 13 dependent therefrom), 28 (claim 29 dependent therefrom), and 30 (claim 31 dependent therefrom) are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The specification discloses that "[t]he medium used for the present invention may be a natural or synthetic medium so long as it contains a carbon source, a nitrogen source, inorganic ions and other trace amount organic constituents as required" (underline added for emphasis; p. 27, lines 9-12 of the specification). As such, that the medium contains a

carbon source, a nitrogen source, inorganic ions, and organic constituents appears to be a necessary element for the production of an L-amino acid or L-lysine.

[d] Claims 16 (claim 17 dependent therefrom) and 20 (claim 21 dependent therefrom) are confusing as it is unclear as to how a protein "has an amino acid sequences of SEQ ID NO:6" or "has an amino acid sequences of SEQ ID NO:10" and simultaneously includes substitution, deletion, insertion, addition or inversion of one or several amino acids. It is suggested that applicants clarify the meaning of the claims.

[e] Claims 17 and 21 are indefinite in the recitation of a "stringent condition" as the specification does not define what conditions constitute "stringent." What hybridization conditions are considered "stringent" varies widely in the art depending on the individual situation as well as the person making the determination. While the specification discloses a "definition" of the term (pp. 35-36 of the specification), it remains unclear as to those nucleic acids that are to be encompassed by the claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[16] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. Claims 1 (claims 12-13 dependent therefrom), 5 (claims 28-29 dependent therefrom), and 7 (claims 2, and 30-31 dependent therefrom) are drawn to a strain of *Methylophilus methylotrophus* having enhanced dihydrodipicolinate synthase activity and/or aspartokinase activity as compared to a corresponding wild type strain and optionally wherein the strain has an additional enhanced activity or activities of recited enzymes (claims 8-10 and 26-27). Claims 16-17 are drawn to (in relevant part) a genus of variants of SEQ ID NO:5 encoding a protein having aspartokinase activity. Claims 20-21 are drawn to (in relevant part) a genus of variants of SEQ ID NO:9 encoding a protein having dihydrodipicolinate synthase activity.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Regarding claim 1, the specification discloses only a single representative species of the genus of isolated *M. methylotrophus* strains, *i.e.,* a *M. methylotrophus* host cell transformed with an expression vector encoding SEQ ID NO:10. The genus of strains encompasses species that have any modification(s) that results in enhanced dihydrodipicolinate synthase activity. The genus encompasses widely variant species, including (but not limited to) alterations to the dihydrodipicolinate synthase polypeptide sequence and/or alterations to the endogenous promoter and/or enhancer sequence(s) of the dihydrodipicolinate synthase gene. Similar reasoning applies to the genus of strains of claims 5, 7-10, and 26-27.

Regarding claims 16 and 20, the specification fails to disclose even a single representative species of the genus of DNAs of part (B) of claim 16 or part (F) of claim 20. Regarding claims 17 and 21, the specification discloses only a single representative species of the genus of claimed DNAs of part (b) of claim 17, *i.e.,* SEQ ID NO:5, or the genus of claimed DNAs of part (f) of claim 21, *i.e.,* SEQ ID NO:9. The genus of DNAs encompasses widely variant species, including (but not limited to) DNAs encoding any variant of SEQ ID NO:6 having aspartokinase activity or any variant of SEQ ID NO:10 having dihydrodipicolinate synthase activity.

While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the claimed genus of isolated *M. methylotrophus* strains or DNAs

encompasses species that are widely variant as described above. Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[17] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding SEQ ID NO:6 or 10, a *M. methylophilus* host cell transformed with an expression vector encoding SEQ ID NO:6 and/or 10, and a method for making L-lysine using said host cell, does not reasonably provide enablement for the broad scope of claimed *M. methylophilus* strains having enhanced enzyme activity or activities, a method of making any L-amino acid using said strain, all variants of SEQ ID NO:5 encoding a protein having aspartokinase activity, and all variants of SEQ ID NO:9 encoding a protein having dihydrodipicolinate synthase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C)

The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

(A) The breadth of the claims: Regarding claims 1 (claim(s) 2 and 12-13 dependent therefrom), 5 (claim(s) 28-29 dependent therefrom) and 7 (claim(s) 30-31 dependent therefrom), 8-10, and 26-27, the claims are so broad as to encompass an isolated *M. methylotrophus* strain having any modification such that dihydrodipicolinate synthase and/or aspartokinase activity are enhanced and optionally wherein the activities of dihydrodipicolinate reductase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase activities are enhanced by any modification(s). Claim 30 (claim 31 dependent therefrom) is so broad as to encompass a method for making any L-amino acid using the strain of claim 7. Regarding claims 1 part b), 5 part b), 7 part b), 16 part (B), 17 part (b), 20 part (F), and 21 part (f), the claims broadly encompass variants of SEQ ID NO:9 and 10. The enablement provided by the specification is not commensurate with the scope of the claims with regard to modification(s) that result in enhanced enzyme activity and variants of SEQ ID NO:9 and 5 as encompassed by the claims. In this case the disclosure is limited to an isolated DNA encoding SEQ ID NO:6 or 10 and a *M. methylophilus* host cell transformed with an expression vector encoding SEQ ID NO:6 and/or 10, and a method for making an L-amino acid using said host cell.

(B) The nature of the invention: Applicants' disclosure describes the use of a *M. methylophilus* host cell transformed with expression vectors encoding the dihydrodipicolinate synthase of SEQ ID NO:10 or the aspartokinase of SEQ ID NO:6 for the production of an L-lysine.

(C) The state of the prior art; (D) The level of one of ordinary skill; and (E) The level of predictability in the art: At the time of the invention, the use of *M. methylophilus* as a host for recombinant protein expression was well known in the art (see, *e.g.,* Barth et al., EP 0037273; cited in the IDS filed 1/10/2002). However, while methods of modifying an encoding nucleic acid sequence were well known in the art at the time of the invention, the examiner can find no teaching or suggestion in the prior art of record directed to nucleic acids encoding the dihydrodipicolinate synthase of SEQ ID NO:10 and the aspartokinase of SEQ ID NO:6 or variants thereof. The encoded amino acid sequence of a polypeptide determines the protein's structural and functional properties. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which nucleotides in the encoding nucleic acid or amino acids in the encoded protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one

skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given nucleic acid were known in the art. However, the state of the art at the time of the invention provides no guidance for altering the polypeptide of SEQ ID NO:10 or 6 with an expectation of obtaining a polypeptide that has the desired activity, *i.e.,* enhanced aspartokinase or dihydrodipicolinate synthase activity with the ability to increase production of L-lysine. The state of the art at the time of the invention provides evidence for the high level of unpredictability in altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York; cited in the Office action mailed 7/23/2004) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are evidenced by the reference of Witkowski et al. (*Biochemistry* 38:11643-11650; cited in the Office action mailed 7/23/2004), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647).

(F) The amount of direction provided by the inventor and (G) The existence of working examples: The specification discloses only a single working example of DNAs encoding SEQ ID NO:6 or variants thereof, *i.e.,* SEQ ID NO:5 and discloses only a single working example of DNAs encoding SEQ ID NO:10 or variants thereof, *i.e.,* SEQ ID NO:9 (see, *e.g.,* pp. 58-60 and 62-64 of the instant specification). However, the specification fails to disclose even a single working example of variants of SEQ ID NO:5 or 9 that encode polypeptides that maintain aspartokinase or dihydrodipicolinate synthase activity, respectively or specific guidance for production thereof. While the specification fails to disclose even a single working example of the claimed *M. methylophilus* strains, one of skill in the art would reasonably expect vector-driven overexpression of nucleic acids encoding SEQ ID NO:6 and/or 10 in a *M. methylophilus* host cell would result in increased activity of SEQ ID NO:6 and/or 10 and that such host cells could be used for the production of any L-lysine. Other than increasing enzyme activity by vector-driven overexpression of an enzyme, the specification fails to disclose other methods by which a skilled artisan can enhance an enzyme's activity.

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of enhancing the overall activity of an enzyme in a host cell by increasing expression of the enzyme in a host cell by transformation of the host cell with an expression vector encoding the enzyme were known in the art at the time of the invention, it was not routine in the art to attempt all methods to promote enhancement of a given enzyme's activity for increased production of any L-amino acid. Also, while methods of isolating or generating variants of a given

nucleic acid were known in the art at the time of the invention, *e.g.,* site-directed mutagenesis, it was not routine in the art to screen for all nucleic acids having a substantial number of substitutions or modifications as encompassed by the claims and screen and isolate those nucleic acids encoding polypeptides that have the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[18] Claims 16-17 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Kojima et al. (WO 95/16042; cited in the IDS filed 9/5/2003).

Claims 16-17 are drawn to (in relevant part) a DNA encoding a variant of SEQ ID NO:6 having aspartokinase activity (claim 16), wherein the DNA is hybridizable to nucleotides 510-1736 of SEQ ID NO:5 or a part thereof (claim 17). Claims 20-21 are drawn to (in relevant part) a DNA encoding a variant of SEQ ID NO:10 having dihydrodipicolinate synthase activity (claim 20), wherein the DNA is hybridizable to nucleotides 1268-2155 of SEQ ID NO:9 or a part thereof (claim 21).

Kojima et al. teaches a DNA encoding a polypeptide having aspartokinase activity (pp. 70-72) and a DNA encoding a polypeptide having dihydrodipicolinate synthase activity (pp. 65-66). This anticipates claims 16-17 and 20-21 as written.

Conclusion

[19] Status of the claims:

Claims 1-2, 5, 7-10, and 12-31 are pending.

Claims 14-15, 18-19, and 22-25 are withdrawn from consideration.

Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Thursday and alternate Fridays from 6:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are

unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (571) 273-8300. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

03-16-05

DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER